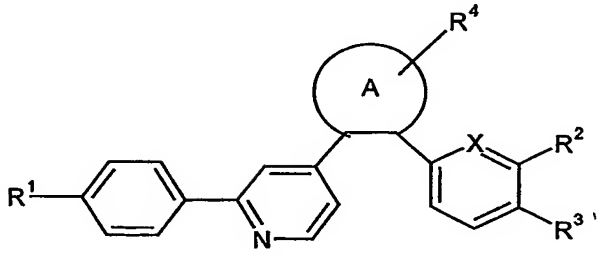
Claims

1 A compound of formula (I), a pharmaceutically acceptable salt, solvate or derivative thereof:



(I)

wherein

A is furan, dioxolane, thiophene, pyrrole, imidazole, pyrrolidine, pyran, pyridine, pyrimidine, morpholine, piperidine, oxazole, isoxazole, oxazoline, oxazolidine, thiazole, isothiazole, thiadiazole, benzofuran, indole, isoindole, indazole, imidazopyridine, quinazoline, quinoline, isoquinoline, pyrazole or triazole;

X is N or CH;

R^1 is hydrogen, C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkoxy, halo, cyano, perfluoro C_{1-6}alkyl, perfluoroC_{1-6}alkoxy, $-NR^5R^6$, $-(CH_2)_nNR^5R^6$, $-O(CH_2)_nOR^7$, $-O(CH_2)_n$-Het, $-O(CH_2)_nNR^5R^6$, $-CONR^5R^6$, $-CO(CH_2)_nNR^5R^6$, $-SO_2R^7$, $-SO_2NR^5R^6$, $-NR^5SO_2R^7$, $-NR^5COR^7$, $-O(CH_2)_nCONR^5R^6$, $-NR^5CO(CH_2)_nNR^5R^6$ or $-C(O)R^7$;

R^2 is hydrogen, C_{1-6}alkyl, halo, cyano or perfluoroC_{1-6}alkyl;

R^3 is hydrogen or halo;

R^4 is hydrogen, halo, phenyl, C_{1-6}alkyl or $-NR^5R^6$;

where

R^5 and R^6 are independently selected from hydrogen; Het; C_{3-6}cycloalkyl optionally substituted by C_{1-6}alkyl; or by C_{1-6}alkyl optionally substituted by Het, alkoxy, cyano or $-NR^aR^b$ (where R^a and R^b which may the same or different are hydrogen or C_{1-6}alkyl, or R^a and R^b together with the nitrogen atom to which they are attached may form a 4,5 or 6-membered saturated ring); or R^5 and R^6 together with the nitrogen atom to which they are attached form a 3, 4, 5, 6 or 7-membered saturated or unsaturated ring which may contain one or more heteroatoms selected from N, S or O, and wherein the ring may be

further substituted by one or more substituents selected from halo (such as fluoro, chloro, bromo), cyano, -CF_3, hydroxy, –OCF_3, C_{1-6}alkyl and C_{1-6}alkoxy;

R^7 is selected from hydrogen and C_{1-6}alkyl;

Het is a 5 or 6-membered C-linked heterocyclyl group which may be saturated, unsaturated or aromatic, which may contain one or more heteroatoms selected from N, S or O and which may be substituted by C_{1-6}alkyl; and

n is 1-4;

with the provisos that :

a) when A is thiazole (wherein the thiazole sulfur is on the same side as the 4-pyridyl moiety); X is N; R^1 is hydrogen, C_{1-6}alkyl, C_{1-6}alkoxy, halo, cyano, perfluoroC_{1-6}alkyl or perfluoroC_{1-6}alkoxy; R^2 is hydrogen, C_{1-6}alkyl, halo, cyano or perfluoroC_{1-6}alkyl; and R^3 is hydrogen or halo; then R^4 is not NH_2; and

b) when X is N, A is pyrazole (where the ring containing X is attached to the pyrazole ring at carbon atom next to a pyrazole ring nitrogen), R^2 is hydrogen then R^3 is not hydrogen.

2 A compound according to any preceding claim wherein A is imidazole optionally substituted by one R^4 substitutent.

3 A compound according to any preceding claim wherein X is N.

4 A compound according to any preceding claim wherein R^1 is C_{1-6}alkyl, C_{1-6}alkoxy, halo, cyano, perfluoroC_{1-6}alkoxy, -NR^5R^6, -$(CH_2)_nNR^5R^6$, -$O(CH_2)_nOR^7$, -$O(CH_2)_n$-Het, -$O(CH_2)_nNR^5R^6$, -$CONR^5R^6$, -SO_2R^7, -$NR^5SO_2R^7$, -NR^5COR^7, -$O(CH_2)_nCONR^5R^6$, -$NR^5CO(CH_2)_nNR^5R^6$ or -$C(O)R^7$.

5 A compound according to any preceding claim wherein R^2 is hydrogen, C_{1-6}alkyl or fluoro.

6 A compound according to any preceding claim wherein R^3 is hydrogen.

7 A compound according to any preceding claim wherein R^4 is hydrogen, phenyl, C_{1-6}alkyl or halo.

8 A compound according to any preceding claim wherein R^5 and R^6 are independently selected from hydrogen; Het; C_{3-6}cycloalkyl optionally substituted by C_{1-6}alkyl; or by C_{1-6}alkyl optionally substituted by Het, alkoxy, cyano or $-NR^aR^b$ (where R^a and R^b which may the same or different are hydrogen or C_{1-6}alkyl, or R^a and R^b together with the nitrogen atom to which they are attached may form a 4, 5 or 6-membered saturated ring); or R^5 and R^6 together with the atom to which they are attached form a morpholine, piperidine, pyrrolidine or piperazine ring, each of which may be substituted by halo (such as fluoro, chloro, bromo), cyano, $-CF_3$, hydroxy, $-OCF_3$, C_{1-4}alkyl or C_{1-4}alkoxy.

9 A compound according to claim 1 wherein

A is imidazole;

X is N;

R^1 is C_{1-6}alkyl, C_{1-6}alkoxy, halo, cyano, perfluoroC_{1-6}alkoxy, $-NR^5R^6$, $-(CH_2)_nNR^5R^6$, $-(CH_2)_nOR^7$, $-O(CH_2)_n$-Het, $-O(CH_2)_nNR^5R^6$, $-CONR^5R^6$, $-SO_2R^7$, $-NR^5SO_2R^7$, $-R^5COR^7$, $-O(CH_2)_nCONR^5R^6$, $-NR^5CO(CH_2)_nNR^5R^6$ or $-C(O)R^7$;

R^2 is hydrogen, C_{1-6}alkyl or fluoro;

R^3 is hydrogen or halo;

R^4 is hydrogen, phenyl, C_{1-6}alkyl or halo;

R^5 and R^6 are independently selected from hydrogen, Het or C_{1-6}alkyl; or R^5 and R^6 together with the atom to which they are attached form a morpholine, piperidine, pyrrolidine or piperazine ring, each of which may be substituted by halo (such as fluoro, chloro, bromo), cyano, $-CF_3$, hydroxy, $-OCF_3$, C_{1-4}alkyl or C_{1-4}alkoxy;

R^7 is selected from hydrogen and C_{1-6}alkyl;

Het is a 5 or 6-membered C-linked heterocyclyl group which may be saturated, unsaturated or aromatic, which may contain one or more heteroatoms selected from N, S or O and which may be substituted by C_{1-6}alkyl; and

n is 1-4.

10 A compound according to claim 1 wherein the compound is selected from the list:

4-{2-*tert*-Butyl-5-[6-methyl]-pyridin-2-yl-1*H*-imidazol-4-yl}-2-(4-methanesulfonyl-phenyl)-pyridine (Example 84);

4-{4-[4-(2-*tert*-Butyl-5-{6-methyl}-pyridin-2-yl-1*H*-imidazol-4-yl)-pyridin-2-yl]-phenyl}-morpholine (Example 86);

N-(tetrahydropyran-4-yl)-4-(4-{2-isopropyl-5-[6-methyl-pyridin-2-yl]-1*H*-imidazol-4-yl}-pyridin-2-yl)-benzamide (Example 96);

4-{4-[4-(2-isopropyl-5-{6-methyl}-pyridin-2-yl-1*H*-imidazol-4-yl)-pyridin-2-yl]-phenyl}-morpholine (Example 97);

4-(4-{4-[2-Isopropyl-5-(6-methyl-pyridin-2-yl)-1*H*-imidazol-4-yl]-pyridin-2-yl}-benzyl)- dimethyl-amine (Example 105);

4-(4-{4-[2-Isopropyl-5-(6-methyl-pyridin-2-yl)-1*H*-imidazol-4-yl]-pyridin-2-yl}-benzyl)-morpholine (Example 104);

N-(tetrahydropyran-4-yl)-4-(4-{2-*tert*-Butyl-5-[6-methyl-pyridin-2-yl]-1*H*-imidazol-4-yl}-pyridin-2-yl)-benzamide (Example 81);

(4-{4-[2-*tert*-Butyl-5-(6-methyl-pyridin-2-yl)-1*H*-imidazol-4-yl]-pyridin-2-yl}-benzyl)-pyrrolidine (Example 103);

4-(2-*tert*-Butyl-5-{6-methyl}-pyridin-2-yl-1*H*-imidazol-4-yl)-2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-pyridine (Example 108); and

4-{4-[4-(2-methyl-5-{6-methyl}-pyridin-2-yl-1*H*-imidazol-4-yl)-pyridin-2-yl]-phenyl}-morpholine (Example 98);

and pharmaceutically acceptable salts, solvates and derivatives thereof.

11 A pharmaceutical composition comprising a compound defined in any preceding claim and a pharmaceutically acceptable carrier or diluent.

12 The use of a compound defined in any one of claims 1 to 10 in the manufacture of a medicament for the treatment or prophylaxis of a disorder mediated by the ALK5 receptor in mammals.

13 The use according to claim 12 wherein the disorder is selected from chronic renal disease, acute renal disease, wound healing, arthritis, osteoporosis, kidney disease, congestive heart failure, ulcers, ocular disorders, corneal wounds, diabetic nephropathy, impaired neurological function, Alzheimer's disease, atherosclerosis, peritoneal and sub-dermal adhesion, any disease wherein fibrosis is a major component, including, but not limited to lung fibrosis, kidney fibrosis, liver fibrosis [for example, hepatitis B virus (HBV),

hepatitis C virus (HCV)], alcohol induced hepatitis, retroperitoneal fibrosis, mesenteric fibrosis, haemochromatosis and primary biliary cirrhosis, endometriosis, keloids and restenosis.

14 The use according to claim 13 wherein the disorder is kidney fibrosis.

15 A compound defined in any one of claims 1 to 10 for use as a medicament.